

## REMARKS

In the Office Action, the Examiner withdrew the anticipation rejection against claims 1-13 over Menard et al. (WO 02/09725), withdrew the anticipation rejection against claims 1-5 and 7-12 over Horrobin et al. (US 6,245,811), and withdrew the obviousness rejection against claims 1-16 over Cook et al. (US 6,077,868) in view of Watkins et al. (Journal of the American College of Nutrition 2000, 19:478S-486S). However, the Examiner raised a new enablement rejection against claims 1 and 4-16 under 35 U.S.C. §112, first paragraph and a new obviousness rejection against claims 1-16 under 35 U.S.C. §103(a) over Cook et al. (US 6,395,782) in view of Horrobin et al. (US 6,245,811). Each new rejection raised by the Examiner is addressed separately below. In view of the claim amendments noted above and the remarks below, applicants respectfully request reconsideration of the merits of this patent application.

No extension of time is believed to be necessary and no fee is believed to be due in connection with this response. However, if any extension of time is required in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee to Deposit Account No. 17-0055. No other fee is believed to be due in connection with this response. However, if any fee is due in this or any subsequent response, please charge the fee to the same Deposit Account No. 17-0055.

### Enablement rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1 and 4-16 for lack of enablement. In particular, the Examiner alleged that the specification, while being enabling for a method of treating rheumatoid arthritis by administering conjugated linoleic acid (CLA), does not reasonably provide enablement for treating all diseases or conditions caused by type III hypersensitive reactions.

Without agreeing to the rejection, claims 1, 2, and 4 are canceled to facilitate prosecution and applicant reserves the right to pursue the canceled subject matter in a continuation application. Claim 3 directed at treating rheumatoid arthritis in particular has been rewritten in independent form and an observing step is also added. The amendment to claim 3 is supported by the specification (see e.g., the example section of the application wherein an improvement in joint redness and swelling was observed). As amended, all pending claims are limited to treating

rheumatoid arthritis. The enablement rejection is believed to have been overcome by the amendments and withdrawal of the rejection is respectfully requested.

Obviousness rejection under 35 U.S.C. §103 (a)

*1. The Examiner's position.*

The Examiner rejected claims 1-16 as being obvious over Cook et al. (US 6,395,782) in view of Horrobin et al. (US 6,245,811).

With regard to Cook et al., the Examiner alleged that the reference teaches methods of extending the survival time of a human or non-human animal having a disease, thus in need of treatment, characterized by autoimmune complexes by administering an effective amount of conjugated linoleic acid (citing claim 1) and Cook et al. further teach methods suitable for treating rheumatoid arthritis (citing column 3, lines 37-60). See the paragraph bridging pages 6 and 7 of the office action. The Examiner also cited other parts of Cook et al. to allege that various other limitations of the pending claims are taught (the paragraph bridging pages 6 and 7 of the office action).

With respect to Horrobin et al. (US 6,245,811), the Examiner alleged that the reference disclosed a method for treating a disorder (rheumatoid arthritis) comprising administering to a patient in need thereof an effective amount of the compound according to claim 1 where R<sub>1</sub> is an acyl moiety corresponding to an acid (conjugated linoleic acid, CLA), citing column 14 at lines 55-62, column 15 at line 1, and claims 1, 10, and 28. See page 7, lines 5-8 of the office action. Further, the Examiner asserts that said compound is an ester of CLA (page 7, lines 8-9 of the office action). The Examiner also cited other parts of Horrobin et al. to allege that various other limitations of the pending claims are taught (page 7, lines 9-13 of the office action).

Also with respect to Horrobin et al., the Examiner alleged that the reference discloses in claim 28 a method of treating a disorder selected from the group consisting of ... rheumatoid arthritis ... comprising administering to a patient in need thereof an effective amount of the compound of claim 10 and claim 10 recited a compound according to claim 1 where R<sub>1</sub> is an acyl moiety corresponding to ... conjugated linoleic acid (the last paragraph on page 7 of the office action). The Examiner took the position that Horrobin et al. teach or suggest a method of

treating rheumatoid arthritis with a compound containing conjugated linoleic acid (the last paragraph on page 7 of the office action).

The Examiner acknowledges that Cook et al. do not expressly teach a method wherein the conjugated linoleic acid is in the form of an ester of linoleic acid (lines 1-2 on page 8 of the office action). However, the Examiner alleged that it would have been obvious to one of ordinary skill in the art to use an ester of conjugated linoleic acid, as suggested by Horrobin et al., in the method of treating rheumatoid arthritis as taught by Cook et al. (lines 5-8 on page 8 of the office action). The Examiner asserts that one of ordinary skill in the art would have been motivated to do this because Horrobin et al. suggest that esters of conjugated linoleic acid can be used in a method of treating rheumatoid arthritis (lines 9-11 on page 8 of the office action). The Examiner asserts that it is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose (page 8, lines 11-15 of the office action) and a reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings (page 8, lines 15-20 of the office action).

Lastly, the Examiner alleged that it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention (page 9, lines 3-4 of the office action). The Examiner asserts that the present invention is obvious, as evidenced by the cited references, especially in the absence of evidence to the contrary (page 9, lines 5-7 of the office action).

Applicant strongly disagrees with the rejection, especially as to what Cook et al. and Horrobin et al. teach or suggest to one of ordinary skill in the art, and respectfully traverses the rejection below. As discussed above, claims 1, 2, and 4 are canceled and claim 3 has been amended to contain the additional step of observing an improvement in joint redness and swelling in the human or non-human animal.

## *2. The teaching and inference of Cook et al.*

Cook et al. teach that administering conjugated linoleic acid (CLA) to a human or non-human animal having a condition associated with the existence of autoimmune complexes can extend the survival time or reduce body weight wasting of the human or non-human animal.

Cook et al. indicated that such conditions include rheumatoid arthritis. However, Cook et al. did not teach that CLA can reduce the symptoms of arthritis, much less the specific symptom of joint redness and swelling of rheumatoid arthritis, which is the subject matter of the present invention. To clarify this, claim 3 has been amended contain the additional step of "observing an improvement in joint redness and swelling in the human or non-human animal."

In addition, one of ordinary skill in the art would not infer from Cook et al. that CLA can reduce the symptom of joint redness and swelling of rheumatoid arthritis, much less with a reasonable likelihood of success. The fact that an agent can extend the survival time and reduce body weight wasting in a human or non-human animal having a disease associated with the existence of autoimmune complexes such as rheumatoid arthritis does not make it obvious that the agent can treat the symptoms of the disease such as joint redness and swelling. For example, an agent can extend the life span and reduce body weight wasting of the human or non-human animal suffering from the disease by simply improving the feeding behavior or appetite without affecting joint redness and swelling. Therefore, Cook et al. do not teach and one of ordinary skill in the art would not reasonable infer, at least would not infer with a reasonable likelihood of success as required by law, that CLA can reduce the symptoms of rheumatoid arthritis, much less the specific symptom of joint redness and swelling.

### *3. The teaching and inference of Horrobin et al.*

Applicant strongly disagrees with the Examiner's position that Horrobin et al. (US 6,245,811) teach that an ester of conjugated linoleic acid (CLA) can be used to treat rheumatoid arthritis. What Horrobin et al. teach are that an ester of GLA, DGLA, SA and EPA can be used to treat rheumatoid arthritis and an ester of CLA can be used to treat cancer, cardiovascular disease, metabolism diseases, to promote growth of protein-containing tissues and treat related diseases, and to act as an antioxidant and treat related diseases.

Horrobin et al. is not about new activities of any compound. Rather, it is about combining two or more known bioactive compounds into the same molecule to achieve increased lipophilicity (for passing lipid barriers in the body) as well as additive or maybe even synergistic effect (col.1, lines 13-64). In this regard, it relies on compounds with known bioactivities. At the time the Horrobin et al. application was filed (August 18, 1999), CLA was

known to be effective for treating some other diseases, but not rheumatoid arthritis. The specification of Horrobin et al. is consistent with this. For example, Horrobin et al. mentions the treatment of rheumatoid arthritis in connection with one or more of GLA, DGLA, SA and EPA, but not CLA (see column 13, lines 12-16 and 30-31). The only activities specifically mentioned in connection with CLA are, as known in the art at that time, treating or preventing cancer, treating or preventing cardiovascular disease, treating metabolism diseases, promoting growth of protein-containing tissues, and acting as an antioxidant (see column 6, lines 35-39 and column 14, lines 6-10). Horrobin et al. did not present any data to indicate that they discovered a new activity of CLA for treating rheumatoid arthritis.

The sections of Horrobin et al. cited by the Examiner (col. 14 at lines 55-62, col. 15 at line 1, and claims 1, 10, and 28) list a plurality of compounds including, among others, GLA, DGLA, SA, EPA, DHA, and CLA for treating a plurality of diseases including, among others, impotence, male pattern baldness, renal and urinary tract disorders, cancer, cardiovascular disease/disorder, and rheumatoid arthritis (col. 14 at lines 55-62 and 66, col. 15 at lines 1 and 9, and claims 1, 10, and 28). The Examiner seems to read the above sections to mean that any of the compounds listed can treat any of the diseases listed. However, this is not the case. For example, EPA and DHA which are among the bioactive compounds listed are not effective for treating impotence and male pattern baldness which are among the diseases listed, although they are effective for treating some other listed diseases such as renal and urinary tract disorders. Similarly, CLA was not known to be effective for treating rheumatoid arthritis but known to be effective for treating other listed diseases such as cancer and cardiovascular disease. Therefore, the reasonable way of reading of the sections cited by the Examiner would be that a compound can be used to treat one or more diseases listed there for which the compound was known to be effective at the time the Horrobin et al. application was filed but not that a compound can be used to treat all of the diseases listed. This reasonable way of reading the sections does not violate any claim construction rules with respect to claims 1, 10, and 28 cited by the Examiner. Accordingly, given that Horrobin et al. did not specifically disclose or present any data to indicate that they had identified a new activity of CLA for treating rheumatoid arthritis, a skilled artisan would understand that CLA was listed among the bioactive compounds for its known

effects on cancer and cardiovascular disease, but not rheumatoid arthritis for which one or more other compounds that were known to be effective were among the compounds listed.

For the same reasons, one of ordinary skill in the art would not infer from Horrobin et al., much less with a reasonable likelihood of success as required by law, that an ester of CLA can be used to treat rheumatoid arthritis. If this can be inferred, it also means that it can be inferred that an ester of EPA or DHA can be used to treat impotence and male pattern baldness, which is not consistent with the understanding of the art (see details discussed above). Therefore, Horrobin et al. do not teach and one of ordinary skill in the art would not reasonably infer from Horrobin et al. that an ester of CLA can be used to treat rheumatoid arthritis.

#### *4. Evidence to the contrary.*

As discussed in the present application (e.g., paragraphs [00010] and [00011]), type III hypersensitivity such as rheumatoid arthritis is caused by antibody/antigen immune complex deposition, leading to tissue damage and inflammatory reactions. In the case of rheumatoid arthritis, the immune complex is between the auto-antibodies to type II collagen and type II collagen (see e.g., the example section of the application in which anti-type II collagen antibody was injected to induce rheumatoid arthritis). Given that antibody-initiated type III hypersensitivities such as rheumatoid arthritis depend on the production of antibody, it would be counterintuitive to try to use an agent that can increase antibody production for the treatment of rheumatoid arthritis.

At the time the application was filed, there was evidence in the art that CLA can increase antibody production in the body. For example, Sugano et al. have shown that CLA increases immunoglobulin (antibody) production (M. Sugano et al., *Lipids*, 1998, 33:521-527, copy submitted in connection with the previous response). Similarly, Yamasaki et al. have also shown that CLA increases immunoglobulin (antibody) production (M. Yamasaki et al., *J. Nutr.*, 2003, 133:784-788, copy submitted in connection with the previous response). Furthermore, Yang et al. studied the effect of CLA on another auto-antibody immune complex disease, systemic lupus erythematosus, and showed that CLA treatment promoted the earlier appearance of antinuclear antibodies as well as proteinuria (the first clinical sign of renal failure in Lupus due to antinuclear antibody immune complexes). See Figs. 3 and 4 of Yang et al.,

Immunopharmacology and Immunotoxicology, 2000, 22:433-449 (copy submitted in connection with the response filed on April 17, 2006). This body of evidence indicates that CLA may aggravate rather than reduce antibody-initiated type III hypersensitivities such as rheumatoid arthritis that are caused by immune complex deposit.

*5. The pending claims as amended are not obvious.*

Applicant notes that under the new U.S. Supreme Court decision of *KSR Int'l Co. v. Teleflex, Inc.*, NO. 04-1350 (U.S. April 30, 2007), it remains necessary to identify a reason why one of ordinary skill in the art would have combined the prior art elements in a manner as claimed and the analysis should be made explicit (See the USPTO Memorandum of May 3, 2007 from Margaret Focarino, Deputy Commissioner for Patent Operations).

It is acknowledged that a reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings (page 8, lines 15-20 of the office action). However, as discussed in detail above, Cook et al. do not teach and one of ordinary skill in the art would not reasonable infer, at least not with a reasonable likelihood of success as required by law, that conjugated linoleic acid (CLA) can reduce the symptoms of arthritis, much less the specific symptom of joint redness and swelling. Similarly, Horrobin et al. do not teach and one of ordinary skill in the art would not reasonably infer from Horrobin et al. that an ester of CLA can be used to treat rheumatoid arthritis. Therefore, in contrast to the reason provided at lines 11-15 on page 8 of the office action, it is not the case that Cook et al. and Horrobin et al. teach two compositions each of which is useful for the same purpose. Accordingly, the pending claims as amended are not *prima facie* obvious.

Even assuming for the sake of argument that one would have combined Cook et al. with Horrobin et al., the invention arrived would have been different from that of the present application. As discussed in detail above, Cook et al. teach that CLA can be used to extend the survival time or reduce body weight wasting. Nothing in Cook et al. teaches or infers that CLA can relieve the symptoms of rheumatoid arthritis, much less the specific symptom of joint redness and swelling. Also as discussed in detail above, Horrobin et al. teach that an ester of CLA can be used to treat cancer, cardiovascular disease, metabolism diseases, to promote growth of protein-containing tissues and treat related diseases, and to act as an antioxidant and treat

related diseases. Nothing in Horrobin et al. teaches or infers that an ester of CLA can be used to treat rheumatoid arthritis, much less to relieve the specific symptom of joint redness and swelling. Therefore, if Cook et al. and Horrobin et al. are combined, the invention arrived would have been using an ester of CLA to extend the survival time or reduce body weight wasting rather than the subject matter of the amended claims of relieving the specific symptom of joint redness and swelling of rheumatoid arthritis.

Lastly, when evaluating the obviousness of a particular invention, the law requires considering the "whole" of the prior art. See *In re Keller*, 642 F.2d 413, 425 (CCPA 1981) (determining obviousness from "what the combined teachings of the references would have suggested to those of ordinary skill in the art"). "When prior art contains apparently conflicting references, the [PTO] must weigh each reference for its power to suggest solutions to an artisan of ordinary skill." See *In re Young*, 927 F.2d 588, 591 (Fed. Cir. 1991).

As discussed in detail above, Cook et al. and Horrobin et al. do not teach or suggest that CLA can relieve the specific symptom of joint redness and swelling of rheumatoid arthritis. Also as discussed in detail above, there were evidence in the art suggesting that CLA would not be able to relieve the symptom of joint redness and swelling of rheumatoid arthritis. In fact, the evidence suggest just the opposite in that CLA may aggravate rheumatoid arthritis by increasing the production of a component (antibody) of the primary cause of rheumatoid arthritis. When the counter evidence (the three references discussed above and submitted in connection with the responses to previous office actions) are considered together with Cook et al. and Horrobin et al. as required by law for obviousness determinations, it would not have been obvious to a skilled artisan that CLA can be used to relieve the specific symptom of joint redness and swelling of rheumatoid arthritis. At the very least, there would have been sufficient doubt in the mind of a skilled artisan so that a skilled artisan would not have concluded that there would be a reasonable likelihood of success for using CLA to reduce joint redness and swelling of rheumatoid arthritis.

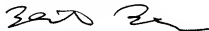
For all the above reasons, it is respectfully submitted that the pending claims as amended are not obvious.



Summary

Having addressed each rejection raised by the Examiner, the claims as amended are believed to be in condition for allowance and a Notice of Allowance is respectfully requested. Should any issues remain outstanding, the Examiner is invited to contact the undersigned at the telephone number appearing below if such would advance the prosecution of this application.

Respectfully submitted,



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